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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,391	06/04/2007	Phanindrudu Aluri	2006 - 021	1959

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EXAMINER	
YU, HONG	

ART UNIT	PAPER NUMBER
1613	

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11/10/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,391	ALURI ET AL.	
	Examiner	Art Unit	
	HONG YU	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,6,7,16-19 and 22-31* is/are pending in the application.

4a) Of the above claim(s) *2,4,6,7,16-19,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/06/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and arguments filed 08/24/2010 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdraw. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application. Applicant has argued both 35 USC 103(a) rejections together and the Examiner will respond accordingly at the end of this action under "Response to Arguments".

Status of claims

Claims 1, 3, 5, 8-15, 20, and 21 have been canceled and claims 2, 4, 6, 7, 16-19, 22, and 23 have been withdrawn. Claims 24-31 are under examination in the instant office action.

New ground of rejections necessitated by Applicant's amendment

The new limitation of "consisting of" in claim 24 necessitates the following new ground of rejections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Nijs (WO 01/26621 A2) in view of Meada et al. (EP 1 209 159 A2) and Jerussi (US 6,489,341 B1) as evidenced by Mirtazapine (Merck Index, 2010, Merck Sharp & Dohme Corp., N.J. [online], retrieved on 11/04/2010. Retrieved from http://www.knovel.com/web/portal/knovel_content?p_p_id=EXT_KNOVEL_CONTENT&p_p_action=1&p_p_state=normal&p_p_mode=view&p_p_col_id=column-1&p_p_col_count=1&_EXT_KNOVEL_CONTENT_struts_action=/ext/knovel_content/view&_EXT_KNOVEL_CONTENT_contentType=2&_EXT_KNOVEL_CONTENT_SpaceID=0&_EXT_KNOVEL_CONTENT_VerticalID=0&_EXT_KNOVEL_CONTENT_SetID=13194496&_EXT_KNOVEL_CONTENT_BookID=1863&_EXT_KNOVEL_CONTENT_NodeID=1885842823&_EXT_KNOVEL_CONTENT_Associated=true&_EXT_KNOVEL_CONTENT_SearchMode=false&sistring=&ststring=).

Applicant's claims

Applicants claim a hard compressed oral disintegrable tablet dosage form consisting of about 1 to 50% by weight of anhydrous mirtazapine with 90% of the anhydrous mirtazapine particles being less than 400 µm, about 10 to 80% by weight of microcrystalline cellulose as a diluent, and 2 to 15% by weight of crospovidone as a dispersing agent, magnesium stearate as a lubricant, sugar as a sweetening agent, lemon, and a flavoring agent (see claims 24-30).

Determination of the Scope and Content of the Prior Art

(MPEP 2141.01)

De Nijs teaches a pharmaceutical composition in form of disintegrating oral tablet comprising mirtazapine (page 2, line 28-30, page 3, line 17, and page 5, line12 through page 6, line 17) and excipients (claim 1).

De Nijs further teaches the excipients being microcrystalline cellulose (diluent), crospovidone (dispersing agent), mannitol and aspartame (sweetening agents), magnesium stearate (lubricant), and flavorants in example (page 9, line 15 and 16).

Although De Nijs does not specify mirtazapine being in anhydrous form, according to Mirtazapine mirtazapine does not contain water, thus the mirtazapine taught by De Nijs must be in anhydrous form.

Ascertainment of the Difference between Scope of the Prior Art and the Claims

MPEP 2141.02)

De Nijs does not teach: i) the composition "consisting of" mirtazapine and a mixture of excipients comprising diluents, dispersing agents, lubricants, flavoring

agents, and sweetening agents; ii) 90% of the anhydrous mirtazapine particles being less than 400 µm; iii) percentages of mirtazapine, diluent, and dispersing agent

The 1st deficiency is cured by the teachings of De Nijs that a composition comparing mirtazapine and excipients.

The 2nd deficiency is cured by Maeda et al. who teach anhydrous mirtazapine with an average particle diameter of from 10 to 50 µm (paragraph 10) being preferable for pharmaceuticals (paragraph 95).

The 3rd deficiency is cured by Jerussi who teaches an oral tablet (column 13, line 60-63) comprising 20% by weight of mirtazapine as an active agent (table 3 and claim 10), 50 to 90% by weight of a diluent (column 15, line 4-12), and 0.5 to 15% by weight of a dispersing agent (column 15, line 13-36).

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP 2142-2143)

Although the composition taught by De Nijs does not use the language "consisting of", the orally disintegrating dosage units contains mirtazapine as the only active agent and additional excipients. Claim 24 recites "excipients comprising", thus, the composition taught by De Nijs meets the limitation in claim 24. A person of ordinary skill in the art would be able to make the composition that consisting of mirtazapine and the recited excipients.

It would have been prima facie obvious at the time of the invention to a person of ordinary skill in the art to combine the teachings in De Nijs and Maeda et al. to use anhydrous mirtazapine with an average particle diameter of from 10 to 50 µm as taught

by Maeda et al. Anhydrous mirtazapine with an average particle diameter of from 10 to 50 μm being preferable in pharmaceutics was well known to a person of ordinary skill in the art at the time of the invention. It is generally considered to be prima facie obvious to specify a component with a specific particle size which is taught by the prior art to be well known and preferable for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for specifying it flows from it having been used in the prior art, and from it being recognized in the prior art as preferable for the same purpose. As shown by the recited teachings, the instant claims are no more than specifying conventional components of an antidepressant. It therefore follows that the instant claims define prima facie obvious subject matter.

It would have been prima facie obvious at the time of the invention to a person of ordinary skill in the art to combine the teachings in De Nijs and Jerussi to specify an oral disintegrable tablet comprising 20% by weight of mirtazapine as active agent, 50 to 90% by weight of diluent, and 0.5 to 15% by weight of dispersing agent. Incorporating 20% by weight of mirtazapine as active agent, 50 to 90% by weight of diluent, and 0.5 to 15% by weight of dispersing agent in a disintegrable oral tablet would have been suggested to a person of ordinary skill in the art at the time of the invention. Furthermore, Jerussi teaches the amount of disintegrant used varies based on the type of formulation and mode of administration and is readily discernible to those of ordinary skill in the art. It is generally considered to be prima facie obvious to specify percentages of mirtazapine, a diluent, and a dispersing agent in a disintegrable oral tablet which are taught by the prior art to be well known and useful for the same purpose in order to form a

composition that is to be used for an identical purpose. The motivation for specifying them flows from their having been used in the prior art, and from their being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, the instant claims are no more than specifying percentages of mirtazapine, a diluent, and a dispersing agent in a disintegrable oral tablet. It therefore follows that the instant claims define prima facie obvious subject matter.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over De Nijs (WO 01/26621 A2) as evidenced by Mirtazapine (Merck Index, 2010, Merck Sharp & Dohme Corp., N.J. [online], retrieved on 11/04/2010. retrieved from http://www.knovel.com/web/portal/knovel_content?p_p_id=EXT_KNOVEL_CONTENT&p_p_action=1&p_p_state=normal&p_p_mode=view&p_p_col_id=column-1&p_p_col_count=1&_EXT_KNOVEL_CONTENT_struts_action=/ext/knovel_content/view&_EXT_KNOVEL_CONTENT_contentType=2&_EXT_KNOVEL_CONTENT_SpaceID=0&_EXT_KNOVEL_CONTENT_VerticalID=0&_EXT_KNOVEL_CONTENT_SetID=13194496&_EXT_KNOVEL_CONTENT_BookID=1863&_EXT_KNOVEL_CONTENT_NodeID=1885842823&_EXT_KNOVEL_CONTENT_Associated=true&_EXT_KNOVEL_CONTENT_SearchMode=false&sistring=&ststring=), Meada et al. (EP 1 209 159 A2), and Jerussi (US 6,489,341 B1) and further in view of Tam et al. (US 6,495,154 B1).

Applicant's claims

Applicants claim the said flavoring agents are orange, etc.

Determination of the Scope and Content of the Prior Art

(MPEP 2141.01)

The teachings of De Nijs, Meada et al., and Jerussi are discussed above and applied in the same manner.

Ascertainment of the Difference between Scope of the Prior Art and the Claims

MPEP 2141.02)

De Nijs does not specify flavor agents being orange.

This deficiency is cured by Tam et al. who teach an oral rapid disintegrating tablet comprising mirtazapine and orange oil as flavorant (column 6, line 60, column 11, line 42-48, claims 52 and 62).

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP 2142-2143)

It would have been prima facie obvious at the time of the invention to a person of ordinary skill in the art to combine the teachings in De Nijs and Tam et al. to specify orange oil as a flavorant. Orange oil was well known as flavorant to a person of ordinary skill in the art at the time of the invention. It is generally considered to be prima facie obvious to specify components which are taught by the prior art to be well known and useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for specifying it flows from its having been used in the prior art, and from its being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the specifying

conventional component of flavorant. It therefore follows that the instant claims define prima facie obvious subject matter.

Response to Arguments:

Applicant's arguments, filed on 03/06/2010, have been fully considered but they are moot in view of new ground of rejections. However the examiner would like to address the following arguments:

Applicants argue that while the composition taught by De Nijs does not release mirtazapine in the mouth with a coating, the claimed compositing releases mirtazapine in the mouth.

However, this argument is not deemed persuasive. The claimed compositing releasing mirtazapine in the mouth is not claimed and a coating is not excluded in the claim.

Applicants further argue that the mirtazapine size taught by Maeda et al. is preferred for pharmaceutical due to high degree of purity.

However, this argument is not deemed persuasive. First of all, the applicants do not exclude the high degree of purity being desirable in the claimed composition. Secondly, to the examiner's understanding, the high purity is due to anhydrous mirtazapine crystal being substantially free of lower alcohol insolubles. Lastly, as long

as the size of mirtazapine having been taught in prior art, it would be obvious for a person with ordinary skill in art to use in a composition.

Applicants argue again that Jerussi does not teach mirtazapine being the only active and being anhydrous and the tablet being disintegrable.

However, this argument is not deemed persuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Jerussi is incorporated to provide the percentages of mirtazapine and excipients in a tablet which varies based on the type of formulation and mode of administration and is readily discernible to those of ordinary skill in the art. With the incorporation of disintegrants, the tablet must be disintegrable tablet, no matter it is specifically indicated by Jerussi or not.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian-Yong Kwon can be reached on 571-272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/H. Y./
Examiner, Art Unit 1613

/Ernst V Arnold/
Primary Examiner, Art Unit 1613